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In re Application of: Constantine Stratakis *et al.*

Serial No.: 09/935,916

Group No.: 1645

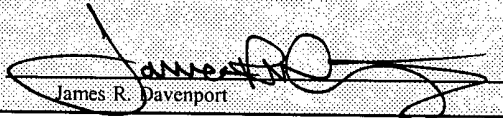
Filed: 08/23/2001

Examiner:

Entitled: **Protein Kinase A And Carney Complex**

**INFORMATION DISCLOSURE
STATEMENT TRANSMITTAL**

Assistant Commissioner for Patents
Washington, D.C. 20231

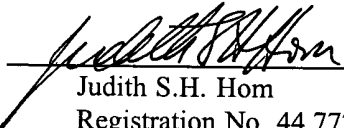
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Dated: <u>July 19, 2002</u>	By:  James R. Davenport

Sir or Madam:

Enclosed please find an Information Disclosure Statement and Form PTO-1449, including copies of the references contained thereon, for filing in the U.S. Patent and Trademark Office.

The Commissioner is hereby authorized to charge any additional fee or credit overpayment to our Deposit Account No. 08-1290. **An originally executed duplicate of this transmittal is enclosed for this purpose.**

Dated: July 19, 2002


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Registration No. 44,772

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By:

James R. Davenport

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following patents are referred to in the body of the specification:

- U.S. Patent No. 5,652,096 issued 7/29/97 to Cimino;
- U.S. Patent No. 4,683,195 issued 7/28/87 to Mullis *et al.*;
- U.S. Patent No. 4,683,202 issued 7/28/87 to Mullis;
- U.S. Patent No. 4,965,188 issued 10/23/90 to Mullis *et al.*;
- U.S. Patent No. 5,322,770 issued 6/21/94 to Gelfand; and
- U.S. Patent No. 4,873,191 issued 10/10/89 to Wagner *et al.*

The following printed publications are referred to in the body of the specification:

- Carney and Young (1992) "Primary Pigmented Nodular Adrenocortical Disease and its Associated Conditions," *Endocrinologist* 2:6-21;

- Carney (1995) "Carney Complex: The Complex of Myxomas, Spotty Pigmentation, Endocrine Overactivity, and Schwannomas," *Semin. Dermatol.* 14:90-98;
- Stratakis *et al.* (1998) "Carney Complex: Diagnosis and Management of the Complex of Spotty Skin Pigmentation, Myxomas, Endocrine Overactivity, and Schwannomas," *Am. J. Med. Genet.*, 80:183-185 (1998);
- Carney *et al.* (1985) "Dominant Inheritance of the Complex of Myxomas, Spotty Pigmentation, and Endocrine Overactivity," *Mayo Clin. Proc.*, 61:165-172;
- Stratakis (2000) "Genetics of Carney Complex and Related Familial Lentiginoses, and Other Multiple Tumor Syndromes," *Frontiers in Biosci.* 5:D353-366;
- Atherton *et al.* (1980) "A syndrome of various cutaneous pigmented lesions, myxoid neurofibromata and atrial myxoma: the NAME syndrome," *Brit. J. Dermatol.* 103:421-429;
- Rhodes *et al.* (1984) "Mucocutaneous lentigines, cardiomucocutaneous myxomas, and multiple blue nevi: The 'LAMB' syndrome," *J. Am. Acad. Dermatol.* 10:72-82;
- Stratakis (2000) "Genetics of Carney Complex and Related Familial Lentiginoses, and Other Multiple Tumor Syndromes," *Pediatr. Pathol. Mol. Med.* 19:41-68;
- Young *et al.* (1989) "Familial Cushing's Syndrome Due to Primary Pigmented Nodular Adrenocortical Disease," *N. Eng. J. Med.* 321:1659-1664;
- Berkhout *et al.* (1989) "Familial Cushing's Syndrome Due to Nodular Adrenocortical Dysplasia is an Inherited Disease of Immunological Origin," *Clin. Endocrinol.* 31:185-191 (1989);
- Stratakis *et al.* (1996) "Carney Complex, a Familial Multiple Neoplasia and Lentiginosis Syndrome," *J. Clin. Invest.* 97:699-705;
- Casey *et al.* (1998) "Identification of a Novel Genetic Locus for Familial Cardiac Myxomas and Carney Complex," *Circul.* 98:2560-2566;

- Stratakis *et al.* (1999) "Paradoxical Response to Dexamethasone in the Diagnosis of Primary Pigmented Nodular Adrenocortical Disease," *Ann. Intern. Med.* 131:585-591;
- Weinstein *et al.* (1991) "Activating Mutations of the Stimulatory G Protein in the McCune-Albright Syndrome," *N. Eng. J. Med.* 325:1688-1695;
- Scott (1991) "Cyclic Nucleotide-Dependent Protein Kinases," *Pharmac. Ther.* 50:123-145;
- Basson *et al.* (1997) "Genetic Heterogeneity of Familial Atrial Myxoma Syndromes (Carney Complex)," *Am. J. Cardiol.* 79: 994-995;
- Taymans *et al.* (1997) "A refined genetic, radiation hybrid and physical map of the Carney complex (CNC) locus on chromosome 2p16; evidence for genetic heterogeneity in the syndrome," *Am. J. Hum. Genet.* 61:A84 (Suppl);
- Liebler *et al.* (1976) "Familial myxomas in four siblings," *J. Thorac. Cardiovasc. Surg.* 71:605-608;
- Tautz (1989) "Hypervariability of simple sequences as a general source for polymorphic DNA markers," *Nucl. Acids Res.* 17:6463-6471;
- Sun *et al.* (1998) "A mutated human homologue to yeast Upf1 protein has a dominant-negative effect on the decay of nonsensecontaining mRNAs in mammalian cells," *Proc. Natl. Acad. Sci. USA* 95:10009-10014;
- Culbertson (1999) "RNA surveillance, unforeseen consequences for gene expression, inherited genetic disorders and cancer," *Trends Genet.*, 15:74-80;
- Maquat (1995) "When cells stop making sense: Effects of nonsense codons on RNA metabolism in vertebrate cells," *RNA* 1:453-465;
- Schwarze *et al.* (2000) "Null Alleles of the *COL5A1* Gene of Type V Collagen Are a Cause of the Classical Forms of Ehlers-Danlos Syndrome (Types I and II)," *Am. J. Hum. Genet.* 66:1757-1765;
- Freddi *et al.* (2000) "Molecular Diagnosis of Stickler Syndrome: A *COL2A1* Stop Codon Mutation Screening Strategy That Is Not Compromised by Mutant mRNA Instability," *Am. J. Med. Genet.* 90:398-406;
- Kozak (1991) "Structural Features in Eukaryotic mRNAs That Modulate the Initiation of Translation," *J. Biol. Chem.* 266:19867-19870;

- DeMarco *et al.* (1996) "Sporadic cardiac myxomas and tumors from patients with Carney complex are not associated with activating mutations of the Gs α Gene," Hum. Genet. 98:185-188;
- Cummings *et al.* (1996) "Genetically lean mice result from targeted disruption of the RII β subunit of protein kinase A," Nature 382:622-626;
- Amieux *et al.* (1997) "Compensatory Regulation of RI α Protein Levels in Protein Kinase A Mutant Mice," J. Biol. Chem. 272:3993-3998;
- Cho *et al.* (2000) "Extracellular protein kinase A as a cancer biomarker: Its expression by tumor cells and reversal by a myristate-lacking C α and RII β subunit overexpression," Proc. Natl. Acad. Sci. USA 97:837-840;
- Beebe *et al.* (1984) "Two Classes of cAMP Analogs Which Are Selective for the Two Different cAMP-binding Sites of Type II Protein Kinase Demonstrate Synergism When Added Together to Intact Adipocytes," J. Biol. Chem. 259:3539-3547;
- Gossen and Bujard (1992) "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters," Proc. Natl. Acad. Sci. USA 89:5547-5551;
- Kistner *et al.* (1996) "Doxycycline-mediated quantitative and tissue-specific control of gene expression in transgenic mice," Proc. Natl. Acad. Sci. USA 93:10933-10938;
- Tarutani *et al.* (1997) "Tissue-specific knockout of the mouse *Pig- α* gene reveals important roles for GPI-anchored proteins in skin development," Proc. Natl. Acad. Sci. USA 94:7400-7405;
- Mazzaferri (1993) "Management of a Solitary Thyroid Nodule," N. Eng. J. Med. 328:553-559;
- Sarlis (2000) "Expression Patterns of Cellular Growth-Controlling Genes in Non-Medullary Thyroid Cancer: Basic Aspects," Rev. Endocrinol. Metab. Dis. 1:183-196;
- Eng (2000) "Editorial: Familial Papillary Thyroid Cancer - Many Syndromes, Too Many Genes," J. Clin. Endocrinol. Metab. 85:1755-1757;

- Farid *et al.* (2000) "Genetics of Follicular Thyroid Cancer," *Endocrinol. Metab. Clin. N. Amer.* 24:865-883;
- Fagin (1997) "Editorial: Familial Nonmedullary Thyroid Carcinoma - the Case for Genetic Susceptibility," *J. Clin. Endocrinol. Metab.* 82:342-344;
- Stratakis *et al.* (1997) "Thyroid Gland Abnormalities in Patients with the Syndrome of Spotty Skin Pigmentation, Myxomas, Endocrine Overactivity, and Schwannomas (Carney Complex)," *J. Clin. Endocrinol. Metab.* 82:2037-2043;
- Ain (1995) "Papillary Thyroid Carcinoma," *Endocrinol. Metab. Clin. N. Amer.* 24:711-760;
- Bier *et al.* (1989) "Multiple Cutaneous Myxomas Coinciding with Repeated Cardiac Myxomas. A syndrome," *Thorac. Cardiovasc. Surg.* 37:317-319;
- Radin and Kempf (1995) "Carney Complex: Report of Three Cases," *Radiol.* 196:383-386;
- Kinzler and Vogelstein (1996) "Lessons from Hereditary Colorectal Cancer," *Cell* 87:159-170;
- Bosman (1999) "The Hamartoma-Adenoma-Carcinoma Sequence," *J. Pathol.* 188:1-2;
- Parma *et al.* (1993) "Somatic mutations in the thyrotropin receptor gene cause hyperfunctioning thyroid adenomas," *Nature* 365:649-651;
- Fuhrer *et al.* (1997) "Somatic Mutations in the Thyrotropin Receptor Gene and Not in the G_s α Protein Gene in 31 Toxic Thyroid Nodules," *J. Clin. Endocrinol. Metab.* 82:3885-3891;
- Esapa *et al.* (1997) "G Protein and Thyrotropin Receptor Mutations in Thyroid Neoplasia," *J. Clin. Endocrinol. Metab.* 82:493-496;
- Russo *et al.* (1995) "Activating mutations of the TSH receptor in differentiated thyroid carcinomas," *Oncogene* 11:1907-1911;
- Pack *et al.* (2000) "Genetic and Histologic studies of Somatomammotropic Pituitary Tumors in Patients with the 'Complex of Spotty Skin Pigmentation, Myxomas, Endocrine Overactivity and Schwannomas,' (Carney Complex)," *J. Clin. Endocrinol. Metab.* 85:3860-3865;

- Bonat *et al.* (2000) "Papillary Thyroid Carcinoma (PTC) in a Child with McCune-Albright Syndrome (MAS): More than a Random Association," Proc. 82nd Ann. Meet. Endocrine Soc., Toronto, Canada, Abstract #P2-2099;
- Fournes *et al.* (1998) "Oncogenic potential of a mutant human thyrotropin receptor expressed in FRTL-5 cells," *Oncogene* 16:985-990;
- Du Villard *et al.* (2000) "Role of the cAMP and MAPK pathways in the transformation of mouse 3T3 fibroblasts by a TSHR gene constitutively activated by point mutation," *Oncogene* 19:4896-4905;
- Michiels *et al.* (1994) "Oncogenic potential of guanine nucleotide stimulatory factor α subunit in thyroid glands of transgenic mice," *Proc. Natl. Acad. Sci. USA* 91:10488-10492;
- Coppee *et al.* (1996) "Early occurrence of metastatic differentiated thyroid carcinomas in transgenic mice expressing the A2a adenosine receptor gene and the human papillomavirus type 16 E7 oncogene," *Oncogene* 13:1471-1482;
- Ledent *et al.* (1997) "Costimulation of Adenylyl Cyclase and Phospholipase C by a Mutant α_{1B} -Adrenergic Receptor Transgene Promotes Malignant Transformation of Thyroid Follicular Cells," *Endocrinol.* 138:369-378;
- Elisei *et al.* (1998) "Genetic and Epigenetic Alterations of the Cyclin-Dependent Kinase Inhibitors p15^{INK4b} and p16^{INK4a} in Human Thyroid Carcinoma Cell Lines and Primary Thyroid Carcinomas," *Cancer* 83:2185-2193;
- Grieco *et al.* (1990) "PTC is a Novel Rearranged Form of the *ret* Proto-Oncogene and is Frequently Detected In Vivo in Human Thyroid Papillary Carcinomas," *Cell* 60:557-563;
- Sozzi *et al.* (1994) "A t(10;17) Translocation Creates the *REP/PTC2* Chimeric Transforming Sequence in Papillary Thyroid Carcinoma," *Genes, Chromosomes & Canc.* 9:244-250;
- Lanzi *et al.* (1992) "Identification of the product of two oncogenic rearranged forms of the *RET* proto-oncogene in papillary thyroid carcinomas," *Oncogene* 7:2189-2194;
- Bongarzone *et al.* (1993) "Molecular Characterization of a Thyroid Tumor-Specific Transforming Sequence Formed by the Fusion of *ret* Tyrosine Kinase

and the Regulatory Subunit RI α of Cyclic AMP-Dependent Protein Kinase A,"
Mol. Cell Biol. 13:358-366;

- Kroll *et al.* (2000) "PAX8-PPAR γ 1 Fusion in Oncogene Human Thyroid Carcinoma," Science 289:1357-1360;
- Ward *et al.* (1998) "Studies of Allelic Loss in Thyroid Tumors Reveal Major Differences in Chromosomal Instability between Papillary and Follicular Carcinomas," J. Clin. Endocrinol. Metab. 83:525-530;
- Kitamura *et al.* (2000) "Allelotyping of Anaplastic Thyroid Carcinoma: Frequent Allelic Losses on 1q, 9p, 11, 17, 19p, and 22q," Genes, Chromosomes & Canc. 27:244-251;
- Gimm *et al.* (2001) "Somatic Mutation and Germline Variants of *MINPP1*, a Phosphatase Gene Located in Proximity to *PTEN* on 10q23.3, in Follicular Thyroid Carcinomas," J. Clin. Endocrinol. Metab. 86:1801-1805;
- Zedenius *et al.* (1996) "Deletions of the long arm of chromosome 10 in progression of follicular thyroid tumors," Hum. Genet. 97:299-303;
- Halachmi *et al.* (1998) "Somatic Mutations of the *PTEN* Tumor Suppressor Gene in Sporadic Follicular Thyroid Tumors," Genes, Chromosomes & Canc. 23:239-243;
- Zhou *et al.* (2000) "Epigenetic PTEN Silencing in Malignant Melanomas without *PTEN* Mutation," Am. J. Pathol. 157:1123-1128;
- Deloukas *et al.* (1998) "A Physical Map of 30,000 Human Genes," Science 282:744-746;
- Yen (2000) "Thyrotropin Receptor Mutations in Thyroid Diseases," Rev. Endocrinol. Metab. Dis. 1:123-129;
- van der Laan *et al.* (1995) "Expression of Growth Factors and Growth Factor Receptors in Normal and Tumorous Human Thyroid Tissues," Thyroid 5:67-73;
- Cetta *et al.* (2000) "Germline Mutations of the APC Gene in Patients with Familial Adenomatous Polyposis-Associated Thyroid Carcinoma: Results from a European Cooperative Study," J. Clin. Endocrinol. Metab. 85:286-292;
- Ho *et al.* (1996) "p53 gene mutation in thyroid carcinoma," Canc. Lett. 103:57-63;

- Belfiore *et al.* (1999) "Insulin/IGF-I hybrid receptors play a major role in IGF-I signaling in thyroid cancer," *Biochimie* 81:403-407;
- Kimura *et al.* (1999) "Expression of Transforming Growth Factor β_1 , β_2 , and β_3 in Multinodular Goiters and Differentiated Thyroid Carcinomas: A Comparative Study," *Thyroid* 9:119-125;
- Delgado and Ganea (2001) "Vasoactive Intestinal peptide and Pituitary Adenylate Cyclase-Activating Polypeptide Inhibit Expression of Fas Ligand in Activated T Lymphocytes by Regulating c-Myc, Nf- κ B, NF-AT, and Early Growth Factors 2/3," *J. Immunol.* 166:1028-1040;
- Ramstad *et al.* (2000) "cAMP-dependent protein kinase (PKA) inhibits T cell activation by phosphorylating Ser-43 of Raf-1 in the MAPK/ERK pathway," *Cell Signal.* 12:557-563;
- Villone *et al.* (2000) "Association between the expression of E1A oncogene and increased sensitivity to growth inhibition induced by sustained levels of cAMP in rat thyroid cells," *Eur. J. Endocrinol.* 142:286-293;
- Richards (2001) "New Signaling Pathways for Hormones and Cyclic Adenosine 3',5'-Monophosphate Action in Endocrine Cells," *Mol. Endocrinol.* 15:209-218;
- Knudson (2000) "Chasing the Cancer Demon," *Ann. Rev. Genet.* 34:1-19;
- Maniatis *et al.* (1987) "Regulation of Inducible and Tissue-Specific Gene Expression," *Science* 236:1237;
- Voss *et al.* (1986) "The Role of Enhancers in the Regulation of Cell-Type Specific Transcriptional Control," *Trends Biochem. Sci.* 11:287;
- Dijkema *et al.* (1985) "Cloning and Expression of the Chromosomal Immune Interferon Gene of the Rat," *EMBO J.* 4:761;
- Uetsuki *et al.* (1989) "Isolation and Characterization of the Human Chromosomal Gene for Polypeptide Chain Elongation Factor-1 α ," *J. Biol. Chem.* 264:5791;
- Kim *et al.* (1990) "Use of the human elongation factor 1 α promoter as a versatile and efficient expression system," *Gene* 91:217;
- Mizushima and Nagata (1990) "pEF-BOS, a powerful mammalian expression vector," *Nuc. Acids. Res.* 18:5322;

- Gorman *et al.* (1982) "The Rous sarcoma virus long terminal repeat is a strong promoter when introduced into a variety of eukaryotic cells by DNA-mediated transfection," *Proc. Natl. Acad. Sci. USA* 79:6777;
- Boshart *et al.* (1985) "A Very Strong Enhancer is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus," *Cell* 41:521;
- Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, New York (1989), pp. 16.7-16.8;
- Smith and Waterman (1981) "Comparison of Biosequences," *Adv. Appl. Math.* 2:482;
- Needleman and Wunsch (1970) "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," *J. Mol. Biol.* 48:443;
- Pearson and Lipman (1988) "Improved tools for biological sequence comparison," *Proc. Natl. Acad. Sci. USA* 85:2444;
- Anderson and Young, Quantitative Filter Hybridization, in *Nucleic Acid Hybridization* (1985);
- Kacian *et al.* (1972) "A Replicating RNA Molecule Suitable for a Detailed Analysis of Extracellular Evolution and Replication," *Proc. Natl. Acad. Sci. USA* 69:3038;
- Chamberlin *et al.* (1970) "New RNA Polymerase from *Escherichia coli* infected with Bacteriophage T7," *Nature* 228:227;
- Wu and Wallace (1989) "The Ligation Amplification Reaction (LAR) - Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Ligation," *Genomics* 4:560;
- Erlich (ed.), *PCR Technology*, Stockton Press (1989);
- Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, NY, pp 9.31-9.58 (1989);
- Sambrook, J. *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, NY, pp 7.39-7.52 (1989);

- Brinster *et al.* (1985) "Factors affecting the efficiency of introducing foreign DNA into mice by microinjecting eggs," Proc. Natl. Acad. Sci. USA 82:4438-4442;
- Hogan *et al.*, in *Manipulating the Mouse Embryo*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1986);
- Jahner *et al.* (1985) "Insertion of the bacterial *gpt* gene into the germ line of mice by retroviral infection," Proc. Natl. Acad. Sci. USA 82:6927-693;
- Stewart *et al.* (1987) "Expression of retroviral vectors in transgenic mice obtained by embryo infection," EMBO J. 6:383-388;
- Jahner *et al.* (1982) "*De novo* methylation and expression of retroviral genomes during mouse embryogenesis," Nature 298:623-628;
- WO 90/08832 (1990);
- Haskell and Bowen (1995) "Efficient Production of Transgenic Cattle by Retroviral Infection of Early Embryos," Mol. Reprod. Dev. 40:386;
- Evans *et al.* (1981) "Establishment in culture of pluripotential cells from mouse embryos," Nature 292:154-156;
- Bradley *et al.* (1984) "Formation of germ-line chimaeras from embryo-derived teratocarcinoma cells lines," Nature 309:255-258;
- Gossler *et al.* (1986) "Transgenesis by means of blastocyst-derived embryonic stem cell lines," Proc. Acad. Sci. USA 83:9065-9069;
- Robertson *et al.* (1986) "Germ-line transmission of genes introduced into cultured pluripotential cells by retroviral vector," Nature 322:445-448;
- Jaenisch (1988) "Transgenic Animals," Science 240:1468-1474;
- Graham and van der Eb (1973) "A New Technique for the Assay of Infectivity of Human Adenovirus 5 DNA," Virol. 52:456;
- Sambrook, J. *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, New York (1989) pp.16.9-16.15;
- Danoff *et al.* (1987) "Adrenocortical Micronodular Dysplasia, Cardiac Myxomas, Lentigines, and Spindle Cell Tumors," Arch. Intern. Med. 147:443-448;

- Stratakis *et al.* (1999) "Genetic Heterogeneity in Carney Complex (OMIM 160980): Contributions of loci at chromosomes 2 and 17 in its genetics," *Am. J. Hum. Genet.* 65:A447;
- Stratakis *et al.* (1996) "Cytogenetic and Microsatellite Alterations in Tumors from Patients with the Syndrome of Myxomas, Spotty Skin Pigmentation, and Endocrine Overactivity (Carney Complex)," *J. Clin. Endocrinol. Metab.* 81:3607-3614;
- Stratakis *et al.* (1998) "Carney Complex, Peutz-Jeghers Syndrome, Cowden Disease, and Bannayan-Zonana Syndrome Share Cutaneous and Endocrine Manifestations, But Not Genetic Loci," *J. Clin. Endocrinol. Metab.*, 83:2972-2976;
- Solberg *et al.* (1997) "The Human Gene for the Regulatory Subunit RI α of Cyclic Adenosine 3',5'-Monophosphate-Dependent Protein Kinase: Two Distinct Promoters Provide Differential Regulation of Alternately Spliced Messenger Ribonucleic Acids," *Endocrinol.* 138:169-181;
- Taymans *et al.* (1999) "Radiation Hybrid Mapping of Chromosomal Region 2p15-p16: Integration of Expressed and Polymorphic Sequence Maps at the Carney Complex (*CNC*) and Doyne Honeycomb Retinal Dystrophy (*DHRD*) Loci," *Genomics* 56:344-349;
- Gyapay *et al.* (1996) "A radiation hybrid map of the human genome," *Hum. Mol. Genet.* 5:339-346;
- Lathrop *et al.* (1984) "Strategies for multilocus linkage analysis in humans," *Proc. Natl. Acad. Sci. USA* 81:3443-3446;
- Sandberg *et al.* (1987) "Molecular Cloning, cDNA Structure and Deduced Amino Acid Sequence for a Type I Regulatory Subunit of cAMP-Dependent Protein Kinase from Human Testis," *Biochem. Biophys. Res. Commun.* 149:939-945;
- Breathnach and Chambon (1981) "Organization and Expression of Eucaryotic Split Genes Coding for Proteins," *Ann. Rev. Biochem.* 50:349-383;

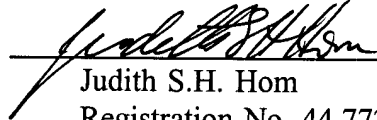
- Kirschner *et al.* (1999) "Genomic Mapping of chromosomal Region 2p15-p21 (D2S378-D2S391): Integration of Genemap'98 within a Framework of Yeast and Bacterial Artificial Chromosomes," *Genomics* 62:21-33;
- O'Donovan *et al.* (1998) "Blind Analysis of Denaturing High-Performance Liquid Chromatography as a Tool for Mutation Detection," *Genomics* 52:44-49;
- Jones *et al.* (1999) "Optimal Temperature Selection for Mutation Detection by Denaturing HPLC and Comparison to Single-Stranded Conformation Polymorphism and Heteroduplex Analysis," *Clin. Chem.*, 45:1133-1140;
- Kuo *et al.* (1970) "Cyclic Nucleotide-Dependent Protein Kinases," *Biochem. Biophys. Acta* 212:79-91;
- Kirschner *et al.* (2000) "Genetic heterogeneity and spectrum of mutations of the PRKAR1A gene in patients with the Carney complex," *Hum. Mol. Genetics* 9:3037-3046;
- Kirschner *et al.* (2000) "Mutations of the gene encoding the protein kinase A type 1- α regulatory subunit in patients with the Carney complex," *Nat. Genet.* 26:89-92; and
- Tarutani *et al.* (1997) "Tissue-specific knockout of the mouse *Pig-a* gene reveals important roles for GPI-anchored proteins in skin development," *Natl. Acad. Sci. USA* 94:7400-7405.

Applicants has become aware of the following printed publications which may be material to the examination of this application:

- Cho-Chung *et al.* (1999) "Antisense DNA-Targeting Protein Kinase A-RIA Subunit: A Novel Approach to Cancer Treatment," *Frontiers in Biosci.* 4:d898-907.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: July 19, 2002



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(Modified)U.S. Department of Commerce
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Serial No.: 09/935,916

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Use Several Sheets If Necessary)

(37 CFR § 1.98(b))

Filing Date: 08/23/01

Group Art Unit:

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Serial / Patent Number	Issue Date	Applicant / Patentee	Class	Subclass	Filing Date
	1	5,652,096	7/29/97	Cimino			
	2	4,683,195	7/28/87	Mullis <i>et al.</i>			
	3	4,683,202	7/28/87	Mullis			
	4	4,965,188	10/23/90	Mullis <i>et al.</i>			
	5	5,322,770	6/21/94	Gelfand			
	6	4,873,191	10/10/89	Wagner <i>et al.</i>			

FOREIGN PATENTS OR PUBLISHED FOREIGN PATENT APPLICATIONS

		Document Number	Publication Date	Country / Patent Office	Class	Subclass	Translation	
							Yes	No
	7	WO90/08832	8/9/90	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

	8	Carney and Young (1992) "Primary Pigmented Nodular Adrenocortical Disease and its Associated Conditions," Endocrinologist 2:6-21
	9	Carney (1995) "Carney Complex: The Complex of Myxomas, Spotty Pigmentation, Endocrine Overactivity, and Schwannomas," Semin. Dermatol. 14:90-98
	10	Stratakis <i>et al.</i> (1998) "Carney Complex: Diagnosis and Management of the Complex of Spotty Skin Pigmentation, Myxomas, Endocrine Overactivity, and Schwannomas," Am. J. Med. Genet., 80:183-185 (1998)
	11	Carney <i>et al.</i> (1985) "Dominant Inheritance of the Complex of Myxomas, Spotty Pigmentation, and Endocrine Overactivity," Mayo Clin. Proc., 61:165-172
	12	Stratakis (2000) "Genetics of Carney Complex and Related Familial Lentiginoses, and Other Multiple Tumor Syndromes," Frontiers in Biosci. 5:D353-366
	13	Atherton <i>et al.</i> (1980) "A syndrome of various cutaneous pigmented lesions, myxoid neurofibromata and atrial myxoma: the NAME syndrome," Brit. J. Dermatol. 103:421-429
	14	Rhodes <i>et al.</i> (1984) "Mucocutaneous lentigines, cardiomucocutaneous myxomas, and multiple blue nevi: The 'LAMB' syndrome," J. Am. Acad. Dermatol. 10:72-82
	15	Stratakis (2000) "Genetics of Carney Complex and Related Familial Lentiginoses, and Other Multiple Tumor Syndromes," Pediatr. Pathol. Mol. Med. 19:41-68
	16	Young <i>et al.</i> (1989) "Familial Cushing's Syndrome Due to Primary Pigmented Nodular Adrenocortical Disease," N. Eng. J. Med. 321:1659-1664
	17	Berkhout <i>et al.</i> (1989) "Familial Cushing's Dyndrome Due to Nodular Adrenocortical Dysplasia is an Inherited Disease of Immunological Origin," Clin. Endocrinol. 31:185-191 (1989)
	18	Stratakis <i>et al.</i> (1996) "Carney Complex, a Familial Multiple Neoplasia and Lentiginosis Syndrome," J. Clin. Invest. 97:699-705
	19	Casey <i>et al.</i> (1998) "Identification of a Novel Genetic Locus for Familial Cardiac Myxomas and Carney Complex," Circul. 98:2560-2566
	20	Stratakis <i>et al.</i> (1999) "Paradoxical Response to Dexamethasone in the Diagnosis of Primary Pigmented Nodular Adrenocortical Disease," Ann. Intern. Med. 131:585-591
	21	Weinstein <i>et al.</i> (1991) "Activating Mutations of the Stimulatory G Protein in the McCune-Albright Syndrome," N. Eng. J. Med. 325:1688-1695
	22	Scott (1991) "Cyclic Nucleotide-Dependent Protein Kinases," Pharmac. Ther. 50:123-145
	23	Basson <i>et al.</i> (1997) "Genetic Heterogeneity of Familial Atrial Myxoma Syndromes (Carney Complex)," Am. J. Cardiol. 79: 994-995

Examiner:

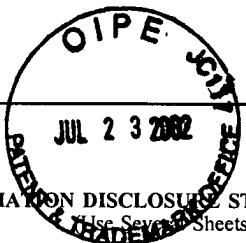
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FORM PTO-1449 (Modified) INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use Several Sheets If Necessary) (37 CFR § 1.98(b))	U.S. Department of Commerce Patent and Trademark Office	Attorney Docket No.: NIH-05098	Serial No.: 09/935,916
	Applicant: Constantine Stratakis <i>et al.</i>		
	Filing Date: 08/23/01	Group Art Unit:	

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)		
24	Taymans <i>et al.</i> (1997) "A refined genetic, radiation hybrid and physical map of the Carney complex (CNC) locus on chromosome 2p16; evidence for genetic heterogeneity in the syndrome," Am. J. Hum. Genet. 61:A84 (Suppl)	
25	Liebler <i>et al.</i> (1976) "Familial myxomas in four siblings," J. Thorac. Cardiovasc. Surg. 71:605-608	
26	Tautz (1989) "Hypervariability of simple sequences as a general source for polymorphic DNA markers," Nucl. Acids Res. 17:6463-6471	
27	Sun <i>et al.</i> (1998) "A mutated human homologue to yeast Upf1 protein has a dominant-negative effect on the decay of nonsensecontaining mRNAs in mammalian cells," Proc. Natl. Acad. Sci. USA 95:10009-10014	
28	Culbertson (1999) "RNA surveillance, unforeseen consequences for gene expression, inherited genetic disorders and cancer," Trends Genet., 15:74-80	
29	Maquat (1995) "When cells stop making sense: Effects of nonsense codons on RNA metabolism in vertebrate cells," RNA 1:453-465	
30	Schwarze <i>et al.</i> (2000) "Null Alleles of the COL5A1 Gene of Type V Collagen Are a Cause of the Classical Forms of Ehlers-Danlos Syndrome (Types I and II)," Am. J. Hum. Genet. 66:1757-1765	
31	Freddi <i>et al.</i> (2000) "Molecular Diagnosis of Stickler Syndrome: A COL2A1 Stop Codon Mutation Screening Strategy That Is Not Compromised by Mutant mRNA Instability," Am. J. Med. Genet. 90:398-406	
32	Kozak (1991) "Structural Features in Eukaryotic mRNAs That Modulate the Initiation of Translation," J. Biol. Chem. 266:19867-19870	
33	DeMarco <i>et al.</i> (1996) "Sporadic cardiac myxomas and tumors from patients with Carney complex are not associated with activating mutations of the Gsα Gene," Hum. Genet. 98:185-188	
34	Cummings <i>et al.</i> (1996) "Genetically lean mice result from targeted disruption of the RIIβ subunit of protein kinase A," Nature 382:622-626	
35	Amieux <i>et al.</i> (1997) "Compensatory Regulation of RIα Protein Levels in Protein Kinase A Mutant Mice," J. Biol. Chem. 272:3993-3998	
36	Cho <i>et al.</i> (2000) "Extracellular protein kinase A as a cancer biomarker: Its expression by tumor cells and reversal by a myristate-lacking Cα and RIIβ subunit overexpression," Proc. Natl. Acad. Sci. USA 97:837-840	
37	Beebe <i>et al.</i> (1984) "Two Classes of cAMP Analogs Which Are Selective for the Two Different cAMP-binding Sites of Type II Protein Kinase Demonstrate Synergism When Added Together to Intact Adipocytes," J. Biol. Chem. 259:3539-3547	
38	Gossen and Bujard (1992) "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters," Proc. Natl. Acad. Sci. USA 89:5547-5551	
39	Kistner <i>et al.</i> (1996) "Doxycycline-mediated quantitative and tissue-specific control of gene expression in transgenic mice," Proc. Natl. Acad. Sci. USA 93:10933-10938	
40	Tarutani <i>et al.</i> (1997) "Tissue-specific knockout of the mouse Pig-α gene reveals important roles for GPI-anchored proteins in skin development," Proc. Natl. Acad. Sci. USA 94:7400-7405	
41	Mazzaferri (1993) "Management of a Solitary Thyroid Nodule," N. Eng. J. Med. 328:553-559	
42	Sarlis (2000) "Expression Patterns of Cellular Growth-Controlling Genes in Non-Medullary Thyroid Cancer: Basic Aspects," Rev. Endocrinol. Metab. Dis. 1:183-196	
43	Eng (2000) "Editorial: Familial Papillary Thyroid Cancer - Many Syndromes, Too Many Genes," J. Clin. Endocrinol. Metab. 85:1755-1757	
44	Farid <i>et al.</i> (2000) "Genetics of Follicular Thyroid Cancer," Endocrinol. Metab. Clin. N. Amer. 24:865-883	
45	Fagin (1997) "Editorial: Familial Nonmedullary Thyroid Carcinoma - the Case for Genetic Susceptibility," J. Clin. Endocrinol. Metab. 82:342-344	
46	Stratakis <i>et al.</i> (1997) "Thyroid Gland Abnormalities in Patients with the Syndrome of Spotty Skin Pigmentation, Myxomas, Endocrine Overactivity, and Schwannomas (Carney Complex)," J. Clin. Endocrinol. Metab. 82:2037-2043	
47	Ain (1995) "Papillary Thyroid Carcinoma," Endocrinol. Metab. Clin. N. Amer. 24:711-760	
48	Bier <i>et al.</i> (1989) "Multiple Cutaneous Myxomas Coinciding with Repeated Cardiac Myxomas. A syndrome," Thorac. Cardiovasc. Surg. 37:317-319	

Examiner:	Date Considered:
-----------	------------------

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

- | | |
|----|---|
| 49 | Radin and Kempf (1995) "Carney Complex: Report of Three Cases," Radiol. 196:383-386 |
| 50 | Kinzler and Vogelstein (1996) "Lessons from Hereditary Colorectal Cancer," Cell 87:159-170 |
| 51 | Bosman (1999) "The Hamartoma-Adenoma-Carcinoma Sequence," J. Pathol. 188:1-2 |
| 52 | Parma <i>et al.</i> (1993) "Somatic mutations in the thyrotropin receptor gene cause hyperfunctioning thyroid adenomas," Nature 365:649-651 |
| 53 | Fuhrer <i>et al.</i> (1997) "Somatic Mutations in the Thyrotropin Receptor Gene and Not in the G _s α Protein Gene in 31 Toxic Thyroid Nodules," J. Clin. Endocrinol. Metab. 82:3885-3891 |
| 54 | Esapa <i>et al.</i> (1997) "G Protein and Thyrotropin Receptor Mutations in Thyroid Neoplasia," J. Clin. Endocrinol. Metab. 82:493-496 |
| 55 | Russo <i>et al.</i> (1995) "Activating mutations of the TSH receptor in differentiated thyroid carcinomas," Oncogene 11:1907-1911 |
| 56 | Pack <i>et al.</i> (2000) "Genetic and Histologic studies of Somatomammotrophic Pituitary Tumors in Patients with the 'Complex of Spotty Skin Pigmentation, Myxomas, Endocrine Overactivity and Schwannomas,' (Carney Complex)," J. Clin. Endocrinol. Metab. 85:3860-3865 |
| 57 | Bonat <i>et al.</i> (2000) "Papillary Thyroid Carcinoma (PTC) in a Child with McCune-Albright Syndrome (MAS): More than a Random Association," Proc. 82nd Ann. Meet. Endocrine Soc., Toronto, Canada, Abstract #P2-2099 |
| 58 | Fournes <i>et al.</i> (1998) "Oncogenic potential of a mutant human thyrotropin receptor expressed in FRTL-5 cells," Oncogene 16:985-990 |
| 59 | Du Villard <i>et al.</i> (2000) "Role of the cAMP and MAPK pathways in the transformation of mouse 3T3 fibroblasts by a TSHR gene constitutively activated by point mutation," Oncogene 19:4896-4905 |
| 60 | Michiels <i>et al.</i> (1994) "Oncogenic potential of guanine nucleotide stimulatory factor α subunit in thyroid glands of transgenic mice," Proc. Natl. Acad. Sci. USA 91:10488-10492 |
| 61 | Coppee <i>et al.</i> (1996) "Early occurrence of metastatic differentiated thyroid carcinomas in transgenic mice expressing the A2a adenosine receptor gene and the human papillomavirus type 16 E7 oncogene," Oncogene 13:1471-1482 |
| 62 | Ledent <i>et al.</i> (1997) "Costimulation of Adenylyl Cyclase and Phospholipase C by a Mutant α_{1B} -Adrenergic Receptor Transgene Promotes Malignant Transformation of Thyroid Follicular Cells," Endocrinol. 138:369-378 |
| 63 | Elisei <i>et al.</i> (1998) "Genetic and Epigenetic Alterations of the Cyclin-Dependent Kinase Inhibitors p15 ^{INK4b} and p16 ^{INK4a} in Human Thyroid Carcinoma Cell Lines and Primary Thyroid Carcinomas," Cancer 83:2185-2193 |
| 64 | Grieco <i>et al.</i> (1990) "PTC is a Novel Rearranged Form of the <i>ret</i> Proto-Oncogene and is Frequently Detected In Vivo in Human Thyroid Papillary Carcinomas," Cell 60:557-563 |
| 65 | Sozzi <i>et al.</i> (1994) "A t(10;17) Translocation Creates the <i>REP/PTC2</i> Chimeric Transforming Sequence in Papillary Thyroid Carcinoma," Genes, Chromosomes & Canc. 9:244-250 |
| 66 | Lanzi <i>et al.</i> (1992) "Identification of the product of two oncogenic rearranged forms of the <i>RET</i> proto-oncogene in papillary thyroid carcinomas," Oncogene 7:2189-2194 |
| 67 | Bongarzone <i>et al.</i> (1993) "Molecular Characterization of a Thyroid Tumor-Specific Transforming Sequence Formed by the Fusion of <i>ret</i> Tyrosine Kinase and the Regulatory Subunit R1 α of Cyclic AMP-Dependent Protein Kinase A," Mol. Cell Biol. 13:358-366 |
| 68 | Kroll <i>et al.</i> (2000) "PAX8-PPAR γ 1 Fusion in Oncogene Human Thyroid Carcinoma," Science 289:1357-1360 |
| 69 | Ward <i>et al.</i> (1998) "Studies of Allelic Loss in Thyroid Tumors Reveal Major Differences in Chromosomal Instability between Papillary and Follicular Carcinomas," J. Clin. Endocrinol. Metab. 83:525-530 |
| 70 | Kitamura <i>et al.</i> (2000) "Allelotyping of Anaplastic Thyroid Carcinoma: Frequent Allelic Losses on 1q, 9p, 11, 17, 19p, and 22q," Genes, Chromosomes & Canc. 27:244-251 |
| 71 | Gimm <i>et al.</i> (2001) "Somatic Mutation and Germline Variants of <i>MINPP1</i> , a Phosphatase Gene Located in Proximity to <i>PTEN</i> on 10q23.3, in Follicular Thyroid Carcinomas," J. Clin. Endocrinol. Metab. 86:1801-1805 |
| 72 | Zedenius <i>et al.</i> (1996) "Deletions of the long arm of chromosome 10 in progression of follicular thyroid tumors," Hum. Genet. 97:299-303 |
| 73 | Halachmi <i>et al.</i> (1998) "Somatic Mutations of the <i>PTEN</i> Tumor Suppressor Gene in Sporadic Follicular Thyroid Tumors," Genes, Chromosomes & Canc. 23:239-243 |
| 74 | Zhou <i>et al.</i> (2000) "Epigenetic PTEN Silencing in Malignant Melanomas without <i>PTEN</i> Mutation," Am. J. Pathol. 157:1123-1128 |

Examiner:

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Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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(37 CFR § 1.98(b))

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

75	Deloukas <i>et al.</i> (1998) "A Physical Map of 30,000 Human Genes," <i>Science</i> 282:744-746
76	Yen (2000) "Thyrotropin Receptor Mutations in Thyroid Diseases," <i>Rev. Endocrinol. Metab. Dis.</i> 1:123-129
77	van der Laan <i>et al.</i> (1995) "Expression of Growth Factors and Growth Factor Receptors in Normal and Tumorous Human Thyroid Tissues," <i>Thyroid</i> 5:67-73
78	Cetta <i>et al.</i> (2000) "Germline Mutations of the APC Gene in Patients with Familial Adenomatous Polyposis-Associated Thyroid Carcinoma: Results from a European Cooperative Study," <i>J. Clin. Endocrinol. Metab.</i> 85:286-292;
79	Ho <i>et al.</i> (1996) "p53 gene mutation in thyroid carcinoma," <i>Canc. Lett.</i> 103:57-63
80	Belfiore <i>et al.</i> (1999) "Insulin/IGF-I hybrid receptors play a major role in IGF-I signaling in thyroid cancer," <i>Biochimie</i> 81:403-407
81	Kimura <i>et al.</i> (1999) "Expression of Transforming Growth Factor β_1 , β_2 , and β_3 in Multinodular Goiters and Differentiated Thyroid Carcinomas: A Comparative Study," <i>Thyroid</i> 9:119-125
82	Delgado and Ganea (2001) "Vasoactive Intestinal peptide and Pituitary Adenylate Cyclase-Activating Polypeptide Inhibit Expression of Fas Ligand in Activated T Lymphocytes by Regulating c-Myc, $\text{NF-}\kappa\text{B}$, NF-AT , and Early Growth Factors 2/3," <i>J. Immunol.</i> 166:1028-1040
83	Ramstad <i>et al.</i> (2000) "cAMP-dependent protein kinase (PKA) inhibits T cell activation by phosphorylating Ser-43 of Raf-1 in the MAPK/ERK pathway," <i>Cell Signal.</i> 12:557-563
84	Villone <i>et al.</i> (2000) "Association between the expression of E1A oncogene and increased sensitivity to growth inhibition induced by sustained levels of cAMP in rat thyroid cells," <i>Eur. J. Endocrinol.</i> 142:286-293
85	Richards (2001) "New Signaling Pathways for Hormones and Cyclic Adenosine 3',5'-Monophosphate Action in Endocrine Cells," <i>Mol. Endocrinol.</i> 15:209-218
86	Knudson (2000) "Chasing the Cancer Demon," <i>Ann. Rev. Genet.</i> 34:1-19
87	Maniatis <i>et al.</i> (1987) "Regulation of Inducible and Tissue-Specific Gene Expression," <i>Science</i> 236:1237
88	Voss <i>et al.</i> (1986) "The Role of Enhancers in the Regulation of Cell-Type Specific Transcriptional Control," <i>Trends Biochem. Sci.</i> 11:287
89	Dijkema <i>et al.</i> (1985) "Cloning and Expression of the Chromosomal Immune Interferon Gene of the Rat," <i>EMBO J.</i> 4:761
90	Uetsuki <i>et al.</i> (1989) "Isolation and Characterization of the Human Chromosomal Gene for Polypeptide Chain Elongation Factor-1 α ," <i>J. Biol. Chem.</i> 264:5791
91	Kim <i>et al.</i> (1990) "Use of the human elongation factor 1 α promoter as a versatile and efficient expression system," <i>Gene</i> 91:217
92	Mizushima and Nagata (1990) "pEF-BOS, a powerful mammalian expression vector," <i>Nuc. Acids. Res.</i> 18:5322
93	Gorman <i>et al.</i> (1982) "The Rous sarcoma virus long terminal repeat is a strong promoter when introduced into a variety of eukaryotic cells by DNA-mediated transfection," <i>Proc. Natl. Acad. Sci. USA</i> 79:6777
94	Boshart <i>et al.</i> (1985) "A Very Strong Enhancer is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus," <i>Cell</i> 41:521
95	Sambrook <i>et al.</i> , <i>Molecular Cloning: A Laboratory Manual</i> , 2nd ed., Cold Spring Harbor Laboratory Press, New York (1989), pp. 16.7-16.8
96	Smith and Waterman (1981) "Comparison of Biosequences," <i>Adv. Appl. Math.</i> 2:482
97	Needleman and Wunsch (1970) "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," <i>J. Mol. Biol.</i> 48:443
98	Pearson and Lipman (1988) "Improved tools for biological sequence comparison," <i>Proc. Natl. Acad. Sci. USA</i> 85:2444
99	Anderson and Young, <i>Quantitative Filter Hybridization, in Nucleic Acid Hybridization</i> (1985)
100	Kacian <i>et al.</i> (1972) "A Replicating RNA Molecule Suitable for a Detailed Analysis of Extracellular Evolution and Replication," <i>Proc. Natl. Acad. Sci. USA</i> 69:3038

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Filing Date: 08/23/01

Group Art Unit:

(37 CFR § 1.98(b))

101	Chamberlin <i>et al.</i> (1970) "New RNA Polymerase from <i>Escherichia coli</i> infected with Bacteriophage T7," Nature 228:227
102	Wu and Wallace (1989) "The Ligation Amplification Reaction (LAR) - Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Ligation," Genomics 4:560
103	Erllich (ed.), <i>PCR Technology</i> , Stockton Press (1989)
104	Sambrook <i>et al.</i> , <i>Molecular Cloning: A Laboratory Manual</i> , Cold Spring Harbor Press, NY, pp 9.31-9.58 (1989)
105	Sambrook, J. <i>et al.</i> , <i>Molecular Cloning: A Laboratory Manual</i> , Cold Spring Harbor Press, NY, pp 7.39-7.52 (1989)
106	Brinster <i>et al.</i> (1985) "Factors affecting the efficiency of introducing foreign DNA into mice by microinjecting eggs," Proc. Natl. Acad. Sci. USA 82:4438-4442
107	Hogan <i>et al.</i> , in <i>Manipulating the Mouse Embryo</i> , Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1986)
108	Jahner <i>et al.</i> (1985) "Insertion of the bacterial <i>gpt</i> gene into the germ line of mice by retroviral infection," Proc. Natl. Acad. Sci. USA 82:6927-693
109	Stewart <i>et al.</i> (1987) "Expression of retroviral vectors in transgenic mice obtained by embryo infection," EMBO J. 6:383-388
110	Jahner <i>et al.</i> (1982) "De novo methylation and expression of retroviral genomes during mouse embryogenesis," Nature 298:623-628
111	Haskell and Bowen (1995) "Efficient Production of Transgenic Cattle by Retroviral Infection of Early Embryos," Mol. Reprod. Dev. 40:386
112	Evans <i>et al.</i> (1981) "Establishment in culture of pluripotent cells from mouse embryos," Nature 292:154-156
113	Bradley <i>et al.</i> (1984) "Formation of germ-line chimaeras from embryo-derived teratocarcinoma cells lines," Nature 309:255-258
114	Gossler <i>et al.</i> (1986) "Transgenesis by means of blastocyst-derived embryonic stem cell lines," Proc. Acad. Sci. USA 83:9065-9069
115	Robertson <i>et al.</i> (1986) "Germ-line transmission of genes introduced into cultured pluripotent cells by retroviral vector," Nature 322:445-448
116	Jaenisch (1988) "Transgenic Animals," Science 240:1468-1474
117	Graham and van der Eb (1973) "A New Technique for the Assay of Infectivity of Human Adenovirus 5 DNA," Virol. 52:456
118	Sambrook, J. <i>et al.</i> , <i>Molecular Cloning: A Laboratory Manual</i> , 2nd ed., Cold Spring Harbor Laboratory Press, New York (1989) pp.16.9-16.15
119	Danoff <i>et al.</i> (1987) "Adrenocortical Micronodular Dysplasia, Cardiac Myxomas, Lentigines, and Spindle Cell Tumors," Arch. Intern. Med. 147:443-448
120	Stratakis <i>et al.</i> (1999) "Genetic Heterogeneity in Carney Complex (OMIM 160980): Contributions of loci at chromosomes 2 and 17 in its genetics," Am. J. Hum. Genet. 65:A447
121	Stratakis <i>et al.</i> (1996) "Cytogenetic and Microsatellite Alterations in Tumors from Patients with the Syndrome of Myxomas, Spotty Skin Pigmentation, and Endocrine Overactivity (Carney Complex)," J. Clin. Endocrinol. Metab. 81:3607-3614
122	Stratakis <i>et al.</i> (1998) "Carney Complex, Peutz-Jeghers Syndrome, Cowden Disease, and Bannayan-Zonana Syndrome Share Cutaneous and Endocrine Manifestations, But Not Genetic Loci," J. Clin. Endocrinol. Metab., 83:2972-2976
123	Solberg <i>et al.</i> (1997) "The Human Gene for the Regulatory Subunit RI α of Cyclic Adenosine 3',5'-Monophosphate-Dependent Protein Kinase: Two Distinct Promoters Provide Differential Regulation of Alternately Spliced Messenger Ribonucleic Acids," Endocrinol. 138:169-181
124	Taymans <i>et al.</i> (1999) "Radiation Hybrid Mapping of Chromosomal Region 2p15-p16: Integration of Expressed and Polymorphic Sequence Maps at the Carney Complex (<i>CNC</i>) and Doyne Honeycomb Retinal Dystrophy (<i>DHRD</i>) Loci," Genomics 56:344-349
125	Gyapay <i>et al.</i> (1996) "A radiation hybrid map of the human genome," Hum. Mol. Genet. 5:339-346
126	Lathrop <i>et al.</i> (1984) "Strategies for multilocus linkage analysis in humans," Proc. Natl. Acad. Sci. USA 81:3443-3446
127	Sandberg <i>et al.</i> (1987) "Molecular Cloning, cDNA Structure and Deduced Amino Acid Sequence for a Type I Regulatory Subunit of cAMP-Dependent Protein Kinase from Human Testis," Biochem. Biophys. Res. Commun. 149:939-945
128	Breathnach and Chambon (1981) "Organization and Expression of Eucaryotic Split Genes Coding for Proteins," Ann. Rev. Biochem. 50:349-383

Examiner:

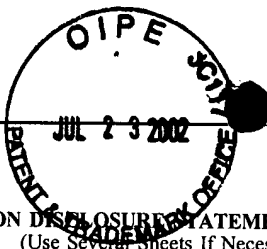
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129	Kirschner <i>et al.</i> (1999) "Genomic Mapping of chromosomal Region 2p15-p21 (D2S378-D2S391): Integration of Genemap'98 within Framework of Yeast and Bacterial Artificial Chromosomes," Genomics 62:21-33
130	O'Donovan <i>et al.</i> (1998) "Blind Analysis of Denaturing High-Performance Liquid Chromatography as a Tool for Mutation Detection," Genomics 52:44-49
131	Jones <i>et al.</i> (1999) "Optimal Temperature Selection for Mutation Detection by Denaturing HPLC and Comparison to Single-Stranded Conformation Polymorphism and Heteroduplex Analysis," Clin. Chem., 45:1133-1140
132	Kuo <i>et al.</i> (1970) "Cyclic Nucleotide-Dependent Protein Kinases," Biochem. Biophys. Acta 212:79-91
133	Kirschner <i>et al.</i> (2000) "Genetic heterogeneity and spectrum of mutations of the PRKAR1A gene in patients with the Carney complex," Hum. Mol. Genetics 9:3037-3046
134	Kirschner <i>et al.</i> (2000) "Mutations of the gene encoding the protein kinase A type 1- α regulatory subunit in patients with the Carney complex," Nat. Genet. 26:89-92
135	Tarutani <i>et al.</i> (1997) "Tissue-specific knockout of the mouse <i>Pig-a</i> gene reveals important roles for GPI-anchored proteins in skin development," Natl. Acad. Sci. USA 94:7400-7405
136	Cho-Chung <i>et al.</i> (1999) "Antisense DNA-Targeting Protein Kinase A-RIA Subunit: A Novel Approach to Cancer Treatment," Frontiers in Biosci. 4:d898-907

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Date Considered:

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